

Appn. No.: 10/521,994
Amendment Dated September 28, 2007
Reply to Office Action of July 2, 2007

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Amendments to the Claims: This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Previously Presented) A modified polyurethane comprising a lipid substituent pendant from at least one urethane nitrogen and/or at least one carbon atom of the modified polyurethane.
2. (Previously Presented) The modified polyurethane of claim 1, wherein the lipid substituent is a steroid lipid substituent.
3. (Previously Presented) The modified polyurethane of claim 1, wherein the steroid lipid substituent is a member selected from the group consisting of a thiol-modified cholesterol substituent, an amino-modified cholesterol substituent, a carboxy-modified cholesterol substituent, and an epoxy-modified cholesterol substituent.
4. (Previously Presented) The modified polyurethane of claim 3, wherein the thiol-modified cholesterol substituent is a 3-mercaptopro-2-hydroxypropyl-cholesterol.
5. (Previously Presented) The modified polyurethane of claim 2, further comprising a linker moiety between (1) the steroid lipid substituent and (2) the at least one urethane nitrogen and/or the at least one carbon atom of the modified polyurethane, wherein the linker moiety covalently binds the steroid lipid substituent with the at least one urethane nitrogen and/or the at least one carbon atom.
6. (Previously Presented) The modified polyurethane of claim 5, wherein the linker moiety is an (n+1)-valent organic radical comprising at least one carbon atom.
7. (Previously Presented) The modified polyurethane of claim 6, wherein the linker moiety is a bivalent organic radical selected from the group consisting of C₁ to C₁₈ alkylene, C₁ to C₁₈ alkyleneamino, C₁ to C₁₈ alkyleneoxy, C₁ to C₁₈ haloalkylene, C₂ to C₁₈ alkenylene, C₆ to C₁₈ arylene, a modified C₂ to C₁₈ alkenylene having at least one carbon substituted by a halogen group, C₂ to C₁₈ alkenylene having one or more O, S, or N atoms incorporated into an alkenylene chain, a bivalent heterocyclic radical, and mixtures thereof.

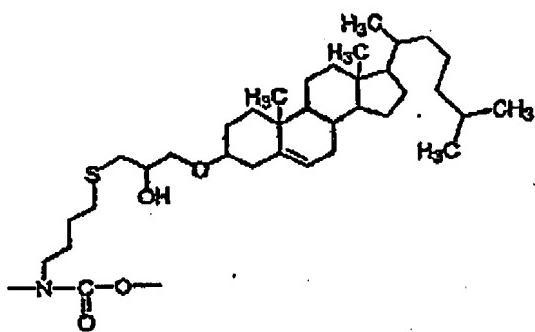
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8. (Previously Presented) The modified polyurethane of claim 7, wherein the linker moiety is C₁ to C₆ alkylene.

9. (Previously Presented) The modified polyurethane of claim 8, wherein the linker moiety is butylene.

10. (Previously Presented) The modified polyurethane of claim 1, wherein the lipid substituent is a thiol-modified cholesterol substituent bound to the at least one urethane nitrogen and wherein said modified polyurethane comprises units having a formula:



11. (Previously Presented) The modified polyurethane of claim 1, wherein the lipid substituent is pendant from about 0.5 to about 50% of urethane nitrogen atoms and/or about 0.5 to about 50% of carbon atoms.

12. (Previously Presented) The modified polyurethane of claim 1, wherein the lipid substituent is pendant from 1 to 20% of urethane nitrogen atoms and/or 1 to 20% of carbon atoms.

13. (Previously Presented) The modified polyurethane of claim 12, wherein the lipid substituent is pendant from 5 to 10% of urethane nitrogen atoms and/or 5 to 10% of carbon atoms.

14. (Previously Presented) The modified polyurethane of claim 1, wherein the modified polyurethane comprises at least about 10 micromoles of the lipid substituent per gram of the modified polyurethane.

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15. (Previously Presented) The modified polyurethane of claim 1, wherein the modified polyurethane has at least two different lipid substituents pendant from urethane nitrogen atoms and/or carbon atoms.

16. (Currently Amended) The modified polyurethane of claim 1, wherein said modified polyurethane ~~is less prone to degradative oxidation~~ exhibits less oxidative degradation than an analogous polyurethane lacking said lipid substituent under the same testing conditions.

17. (Previously Presented) A process for preparing the modified polyurethane of claim 1, the process comprising:

providing a polyurethane comprising a urethane amino moiety and at least one carbon;

providing a multifunctional linker reagent of a formula:



wherein n is an integer from 1 to 3, FG is a functional group selected from the group consisting of a halogen, a carboxyl group, a sulfonate ester, and an epoxy group, LG is a leaving group selected from the group consisting of a halogen, a carboxyl group, a sulfonate ester, and an epoxy group, and R_L is an (n+1)-valent organic radical comprising at least one carbon atom;

providing a lipid comprising the lipid substituent;

reacting the multifunctional linker reagent with the urethane amino moiety to form a polyurethane substituted with at least one substituent group of a formula



reacting the lipid and the polyurethane substituted with the at least one substituent group to form the modified polyurethane.

18. (Previously Presented) The process of claim 17, wherein R_L is a bivalent organic radical selected from the group consisting of C₁ to C₁₈ alkylene, C₁ to C₁₈ alkyleneamino, C₁ to C₁₈ alkyleneoxy, C₁ to C₁₈ haloalkylene, C₂ to C₁₈ alkenylene, C₆ to C₁₈ arylene, a modified C₂ to C₁₈ alkenylene having at least one carbon substituted by a halogen group, C₂ to C₁₈ alkenylene having one or more O, S, or N atoms incorporated into an alkenylene chain, a bivalent heterocyclic radical, and mixtures thereof.

19. (Previously Presented) The process of claim 18, wherein the multifunctional linker reagent is a member selected from the group consisting of a dibromoalkyl compound, a bromo-carboxyalkyl compound, and a bromo-epoxyalkyl compound.

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20. (Previously Presented) The process of claim 17, wherein the lipid comprises a steroid lipid and the lipid substituent comprises a steroid lipid substituent.

21. (Previously Presented) The process of claim 20, wherein the steroid lipid comprises modified cholesterol and the steroid lipid substituent is a member selected from the group consisting of a thiol-modified cholesterol substituent, an amino-modified cholesterol substituent, a carboxy-modified cholesterol substituent, and an epoxy-modified cholesterol substituent.

22. (Previously Presented) The process of claim 21, wherein the modified cholesterol comprises 3-mercaptopropano-2-hydroxypropyl-cholesterol.

23. (Previously Presented) The method of claim 21, comprising preparing the modified cholesterol by contacting a cholesterol with at least one reactant to provide the modified cholesterol having at least one substituent group, wherein the substituent group is a member selected from the group consisting of a thiol group, an amino group, a carboxy group, and an epoxy group.

24. (Previously Presented) The method of claim 23, wherein the cholesterol is treated with epihalohydrin to yield a glycidyl modified cholesterol and the glycidyl modified cholesterol is treated with a thiolating agent to yield a thiol modified cholesterol.

25. (Previously Presented) A process for preparing the modified polyurethane of claim 1, the process comprising:

reacting a steroid lipid with epihalohydrin to yield a glycidyl derivative of the steroid lipid;

reacting the glycidyl derivative of the steroid lipid with a thiolating agent, thereby effecting opening of the glycidyl oxirane group and adding to said lipid molecule a thiol moiety having a protective group bound thereto;

removing said protecting group to produce a thiol-substituted steroid lipid;

reacting a polyurethane with a bi-functional linker comprising a thiol-reactive group, to yield an intermediate polyurethane having a thiol-reactive functional group wherein the thiol-reactive functional group is substituted on said urethane group nitrogen; and

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reacting the thiol-substituted steroid lipid with the intermediate polyurethane having a thiol-reactive functional group to yield the modified polyurethane.

26. (Previously Presented) The process of claim 25, wherein the epihalohydrin is epibromohydrin.

27. (Previously Presented) The process of claim 25, wherein the thiolating agent is selected from the group consisting of thiosulfate, thiourea, trityl mercaptan, tert-butyl mercaptan, thiocyanate, and thioalkanoic acids having 2-6 carbon atoms.

28. (Previously Presented) The process of claim 27, wherein the thiolating agent is thioacetic acid.

29. (Previously Presented) The process of claim 25, wherein the bi-functional linker is a dihaloalkane having 1-12 carbon atoms.

30. (Previously Presented) The process of claim 29, wherein the bi-functional linker is 1,4-dibromobutane.

31. (Currently Amended) A process of producing an implant, said process comprising:

providing the modified polyurethane of claim 1;

forming an article from the modified polyurethane; and

contacting the article with cells to attach the cells to the lipid substituent and thereby

attach the cells to the article to form the implant, provided that a substantial portion of the cells remains attached to the implant when exposed to a fluid-induced sheer stress.

32. (Previously Presented) The process of claim 31, wherein the lipid substituent is a member selected from the group consisting of a thiol-modified cholesterol substituent, an amino-modified cholesterol substituent, a carboxy-modified cholesterol substituent, and an epoxy-modified cholesterol substituent.

33. (Previously Presented) The process of claim 31, wherein the cells are endothelial cells or precursors of endothelial cells.

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34. (Previously Presented) The process of claim 33, wherein the endothelial cells are bovine arterial endothelial cells or blood outgrowth endothelial cells.

35. (Previously Presented) An implant produced by the process of claim 31.

36. (Previously Presented) The implant of claim 35, wherein the implant is a member selected from the group consisting of an artificial heart; cardiac pacer leads; automatic implantable cardiofibrillator leads; a prosthetic heart valve; a cardiopulmonary bypass membrane; a ventricular assist device; an annuloplasty ring; a dermal graft; a vascular graft; a vascular stent; cardiovascular stent; a structural stent; a catheter; a guide wire; a vascular shunt; a cardiovascular shunt; a dura mater graft; a cartilage graft; a cartilage implant; a pericardium graft; a ligament prosthesis; a tendon prosthesis; a urinary bladder prosthesis; a pledget; a suture; a permanently in-dwelling percutaneous device; an artificial joint; an artificial limb; a bionic construct; and a surgical patch.

37. (Previously Presented) The implant of claim 35, wherein the cells are blood outgrowth endothelial cells.

38. (Previously Presented) A method of treating a patient comprising providing the implant of claim 35, wherein the implant is seeded with blood outgrowth endothelial cells.

39. (Previously Presented) A method of treating or preventing a condition in a patient, said method comprising implanting in the patient an implant coated with cells, such that the cells are administered to the patient to treat or prevent the condition, wherein the cells are releasably attached to the implant by a lipid substituent pendant from at least one urethane nitrogen and/or at least one carbon atom of a polyurethane component of the implant.

40. (Previously Presented) The method of claim 39, wherein the condition is at least one of thrombosis and inflammatory cell interactions.